

## PATENT COOPERATION TREATY

## PCT

10/578354

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 27 OCT 2005

WIPO

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Applicant's or agent's file reference pat/gr/kmap	<b>FOR FURTHER ACTION</b>		See Form PCT/PEA/416
International application No. PCT/GR2004/000051	International filing date (day/month/year) 18.10.2004	Priority date (day/month/year) 16.10.2003	
International Patent Classification (IPC) or national classification and IPC C12Q1/68			
Applicant IKONOMOPOULOS, Joannis et al.			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand  16.08.2005		Date of completion of this report  26.10.2005	
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer  Knudsen, H  Telephone No. +49 89 2399-	



**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/GR2004/000051

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

**Description, Pages**

1-16 as originally filed

**Sequence listings part of the description, Pages**

17-18 as originally filed

**Claims, Numbers**

1-10 as originally filed

**Drawings, Sheets**

1/1 as originally filed

- ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-10
	No: Claims	
Inventive step (IS)	Yes: Claims	9
	No: Claims	1-8,10
Industrial applicability (IA)	Yes: Claims	1-10
	No: Claims	

**2. Citations and explanations (Rule 70.7):**

**see separate sheet**

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**Box No. VI Certain documents cited**

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**1. Certain published documents (Rule 70.10)**

and /or

**2. Non-written disclosures (Rule 70.9)**

**see separate sheet**

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**Supplemental Box relating to Sequence Listing**

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**Continuation of Box I, item 2:**

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

a. type of material:

- ☒ a sequence listing
- ☐ table(s) related to the sequence listing

b. format of material:

- ☒ in written format
- ☒ in computer readable form

c. time of filing/furnishing:

- ☒ contained in the international application as filed
- ☐ filed together with the international application in computer readable form
- ☒ furnished subsequently to this Authority for the purposes of search and/or examination
- ☒ received by this Authority as an amendment on

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

**Re Item I**

**Basis of the report**

The sequences SEQ ID Nos: 1 & 2 filed in the sequence listing on paper together with the application differs from the sequences mentioned in claim 1 of the application. The search has been performed for the sequences mentioned in claim 1. The electronically filed sequences are identical to the sequences in the sequence listing.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following document/s/:

- D1: RYAN P ET AL: "PCR detection of Mycobacterium paratuberculosis in Crohn's disease granulomas isolated by laser capture microdissection" GUT, vol. 51, no. 5, November 2002 (2002-11), pages 665-670, XP001205548 ISSN: 0017-5749
- D2: BULL TIM J ET AL: "Characterization of IS900 loci in Mycobacterium avium subsp. paratuberculosis and development of multiplex PCR typing" MICROBIOLOGY, SOCIETY FOR GENERAL MICROBIOLOGY, READING, GB, vol. 146, no. 9, September 2000 (2000-09), pages 2185-2197, XP002173061 ISSN: 1350-0872
- D3: EP-A-1 223 225 (STICHTING NEDERLANDS INSTITUUT VOOR ZUIVELONDERZOEK) 17 July 2002 (2002-07-17)

1. None of the cited documents disclose a primer with the sequence P1N, P2N, P3N or P4N and claims 1-10 are therefore novel.
2. Each of the above documents D1-D3 and a high number of documents that are not cited disclose primers used in PCR and nested PCR which bind within and amplify a portion of the IS900 insertion element of M.avium subsp. paratuberculosis.

The primers P1N, P2N, P3N and P4N do not appear to have any special effect when used alone or in combination with other primers, but show a surprising high sensitivity

and specificity when used in combination in a nested PCR. Thus, the ISA is of the opinion that the problem solved by each of the primers in claim 1 is the provision of an alternative PCR primer binding to IS900.

The design of PCR primers for amplifying a region with a known sequence is considered to belong to the routine tasks which would be obvious to the skilled person wishing to find alternative primers for the amplification of a certain sequence and the ISA therefore finds that each of the primers represent a selection which would be one of the obvious options to the skilled person wishing to provide alternative primers. Thus, claim 1 is not considered inventive.

3. The application does not disclose any surprising specificity or sensitivity of any of the primer combinations of claim 2, apart from the combination employing all 4 primers and claim 2 therefore lacks an inventive step for the same reasons as claim 1.
4. The subject-matter of claims 3-8 and 10 refers to claim 1 and/or 2 and relate to features which are trivial in the field and therefore do not involve an inventive step for the same reasons as claim 1 and/or claim 2.
5. The subject-matter of claim 9 appears to involve an inventive step in view of the surprising sensitivity, reproducibility and specificity (see pages 7-8) compared to prior art PCR tests for detection of MAP. The prior art does not contain any pointer to the use of the specific primers P1N, P2N, P3N and P4N for obtaining a test with improved characteristics and the subject-matter of claim 9 therefore would not be an obvious solution to the skilled person.
6. The subject-matter of claims 1-10 is considered industrially applicable.